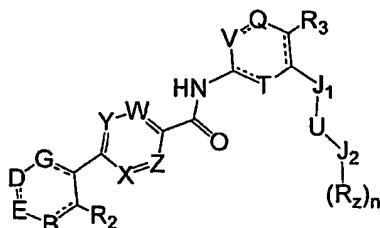


What is claimed is:

1. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

each  $\text{---}$  independently represents a single or double bond;

B and E are independently  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ ,  $\text{NR}_1$  or N; or B and E are taken together to form a fused 5- to 7-membered partially saturated ring that is substituted with from 0 to 3 substituents independently selected from  $\text{R}_1$ ;

D and G are independently  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ ,  $\text{NR}_1$  or N;

W, X, Y and Z are independently  $\text{CR}_1$  or N;

Q, T and V are independently  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ , N or NH; or Q is taken together with V or  $\text{R}_3$  to form a fused 5- to 7-membered carbocycle or heterocycle that is substituted with from 0 to 4 substituents independently selected from  $\text{R}_b$ ;

$\text{R}_1$  is independently chosen at each occurrence from hydrogen, halogen, hydroxy, amino, cyano, nitro, and groups of the formula L-M;

$\text{R}_2$  is halogen, hydroxy, amino, cyano, nitro or a group of the formula L-M;

$\text{R}_3$  is hydrogen, halogen, cyano,  $\text{C}_1\text{-C}_8$ alkyl,  $\text{C}_2\text{-C}_8$ alkenyl,  $\text{C}_2\text{-C}_8$ alkynyl,  $\text{C}_3\text{-C}_8$ cycloalkyl $\text{C}_0\text{-C}_4$ alkyl,  $\text{C}_1\text{-C}_8$ haloalkyl,  $\text{C}_2\text{-C}_8$ alkyl ether,  $\text{C}_1\text{-C}_8$ alkylsulfonyl,  $\text{C}_1\text{-C}_8$ alkylsulfonamido or taken together with Q to form a fused, optionally substituted, 5- to 7-membered carbocycle or heterocycle;

L is independently chosen at each occurrence from a single covalent bond, O,  $\text{C}(=\text{O})$ ,  $\text{OC}(=\text{O})$ ,  $\text{C}(=\text{O})\text{O}$ ,  $\text{OC}(=\text{O})\text{O}$ ,  $\text{S}(\text{O})_m$ ,  $\text{N}(\text{R}_x)$ ,  $\text{C}(=\text{O})\text{N}(\text{R}_x)$ ,  $\text{N}(\text{R}_x)\text{C}(=\text{O})$ ,  $\text{N}(\text{R}_x)\text{S}(\text{O})_m$ ,  $\text{S}(\text{O})_m\text{N}(\text{R}_x)$  and  $\text{N}[\text{S}(\text{O})_m\text{R}_x]\text{S}(\text{O})_m$ ; wherein m is independently selected at each occurrence from 0, 1 and 2; and  $\text{R}_x$  is independently selected at each occurrence from hydrogen and  $\text{C}_1\text{-C}_8$ alkyl;

M is independently selected at each occurrence from (a) hydrogen and hydroxy; and (b)  $\text{C}_1\text{-C}_8$ alkyl,  $\text{C}_2\text{-C}_8$ alkenyl,  $\text{C}_2\text{-C}_8$ alkynyl, mono- and di- $(\text{C}_1\text{-C}_4$ alkyl)amino $\text{C}_0\text{-C}_4$ alkyl, phenyl $\text{C}_0\text{-C}_4$ alkyl,  $\text{C}_3\text{-C}_8$ cycloalkyl $\text{C}_0\text{-C}_4$ alkyl and (5- to 7-membered heterocycloalkyl) $\text{C}_0\text{-C}_4$ alkyl, each of which is substituted with from 0 to 5 substituents independently selected from  $\text{R}_b$ ;

$\text{J}_1$  chosen from O, NH and S;

U is  $\text{C}_1\text{-C}_3$ alkyl, substituted with from 0 to 3 substituents independently chosen from oxo and  $\text{C}_1\text{-C}_3$ alkyl or two substituents are taken together to form a 3- to 7-membered cycloalkyl or heterocycloalkyl;

Either: (a)  $J_2$  is O or S,

n is 1, and

$R_z$  is hydrogen,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ haloalkyl or  $C_2$ - $C_6$ alkyl ether; or

(b)  $J_2$  is N,

n is 2, and

(i)  $R_z$  is independently chosen at each occurrence from hydrogen and  $C_1$ - $C_6$ alkyl substituted with from 0 to 3 substituents selected from  $R_b$ ; or

(ii) both  $R_z$  moieties are joined to form, with  $J_2$ , a 5- to 8-membered heterocycloalkyl that is substituted with from 0 to 3 substituents selected from  $R_b$ ; and

$R_b$  is independently chosen at each occurrence from halogen, hydroxy, cyano, nitro, amino, oxo, COOH,  $C_1$ - $C_6$ alkyl,  $C_3$ - $C_8$ cycloalkyl $C_0$ - $C_4$ alkyl,  $C_1$ - $C_6$ haloalkyl,  $C_1$ - $C_6$ alkoxy,  $C_1$ - $C_6$ haloalkoxy,  $C_2$ - $C_6$ alkyl ether, aminocarbonyl,  $C_1$ - $C_6$ hydroxyalkyl,  $C_1$ - $C_6$ aminoalkyl and mono- and di-( $C_1$ - $C_6$ alkyl)amino.

2. A compound or salt according to claim 1, wherein each  $==$  represents a double bond.

3. A compound or salt according to claim 1 or claim 2, wherein B, E, D, Y and W are CH.

4. A compound or salt according to any one of claims 1-3, wherein T and V are independently N or CH.

5. A compound or salt according to any one of claims 1-4, wherein G is N.

6. A compound or salt according to any one of claims 1-5, wherein  $R_2$  is cyano, nitro, NH<sub>2</sub>, amino,  $C_1$ - $C_4$ alkyl,  $C_1$ - $C_4$ haloalkyl,  $C_1$ - $C_4$ hydroxyalkyl,  $C_1$ - $C_4$ alkoxy,  $C_1$ - $C_4$ alkylthio,  $C_1$ - $C_4$ alkanoyl,  $C_4$ aminoalkyl, mono- or di-( $C_1$ - $C_4$ alkyl)amino $C_0$ - $C_4$ alkyl, ( $C_5$ - $C_6$ cycloalkyl)amino, (5- or 6-membered heterocycloalkyl) $C_0$ - $C_4$ alkyl, - $N(R_x)SO_2C_1$ - $C_4$ alkyl or - $N(SO_2C_1$ - $C_4$ alkyl)<sub>2</sub>.

7. A compound or salt according to claim 6, wherein  $R_2$  is cyano, CHO, amino, nitro,  $C_4$ alkyl,  $C_1$ - $C_4$ haloalkyl,  $C_1$ - $C_4$ alkoxy,  $C_1$ - $C_4$ haloalkoxy,  $C_1$ - $C_4$ alkylthio,  $C_1$ - $C_4$ hydroxyalkyl,  $C_4$ aminoalkyl, mono- and di-( $C_1$ - $C_4$ alkyl)amino $C_0$ - $C_4$ alkyl, oxadiazolyl, cyclopentylamino, - $N(H)SO_2C_4$ alkyl, - $N(CH_3)SO_2C_1$ - $C_4$ alkyl or - $N(SO_2C_1$ - $C_2$ alkyl)<sub>2</sub>.

8. A compound or salt according to claim 7, wherein  $R_2$  is cyano, CHO, amino, nitro, methyl, propyl, hydroxymethyl, trifluoromethyl, methoxy, ethoxy, propoxy, methylthio, ethylthio,  $C_4$ alkylamino, ( $C_1$ - $C_4$ alkyl)aminomethyl, cyclopentylamino, - $N(H)SO_2C_1$ - $C_4$ alkyl, - $N(CH_3)SO_2CH_3$  or  $N(SO_2CH_3)_2$ .

9. A compound or salt according to claim 6, wherein  $R_2$  is halogen, methyl, cyano or trifluoromethyl.

10. A compound or salt according to any one of claims 1-9, wherein  $J_1$  is O.

11. A compound or salt according to any one of claims 1-10, wherein U is  $C_2$ alkyl substituted with from 0 to 2 substituents independently chosen from oxo and  $C_1$ - $C_3$ alkyl.

12. A compound or salt according to claim 11, wherein U is  $-CH_2-CH_2-$ .

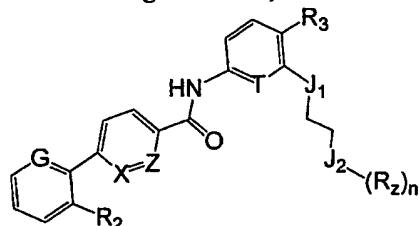
13. A compound or salt according to claim 11, wherein U is  $-CH_2-C(O)-$ .

14. A compound or salt according to any one of claims 1-13, wherein  $-J_2-(R_2)_n$  is chosen from: (i) -OH and -NH<sub>2</sub>, and (ii)  $C_1$ - $C_4$ alkoxy, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl and mono- and di-( $C_1$ - $C_6$ alkyl)amino, each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino,  $C_1$ - $C_4$ alkyl,  $C_1$ - $C_4$ haloalkyl,  $C_1$ - $C_4$ alkoxy,  $C_1$ - $C_4$ haloalkoxy and  $C_1$ - $C_4$ alkylthio.

15. A compound or salt according to any one of claims 1-14, wherein  $R_3$  is halogen,  $C_1$ - $C_4$ alkyl,  $C_2$ - $C_4$ alkyl ether,  $C_1$ - $C_4$ haloalkyl,  $C_1$ - $C_4$ hydroxyalkyl,  $-SO_2CF_3$  or taken together with Q to form a fused 5- or 6-membered carbocycle or heterocycle.

16. A compound or salt according to claim 15, wherein  $R_3$  is halogen, *tert*-butyl or trifluoromethyl.

17. A compound or salt according to claim 1, wherein the compound has the formula:



wherein:

G and T are independently CH or N;

$R_2$  is cyano, CHO, amino, nitro, methyl, ethyl, propyl, trifluoromethyl, methoxy, ethoxy, propoxy methylthio, ethylthio,  $-N(H)SO_2C_1-C_4$ alkyl,  $-N(CH_3)SO_2C_1-C_4$ alkyl or  $-N(SO_2CH_3)_2$ ;

$R_3$  is halogen, cyano,  $C_1$ - $C_6$ alkyl or  $C_1$ - $C_6$ haloalkyl;

X and Z are independently N, CH, C-OH, C-NH<sub>2</sub>, C( $C_1$ - $C_3$ alkyl) or C( $C_1$ - $C_3$ haloalkyl);

$J_1$  is O or NH; and

$-J_2-(R_2)_n$  is chosen from: (i)  $-OH$  and  $-NH_2$ , and (ii)  $C_1-C_4$ alkoxy, pyrrolidinyl, piperidinyl, piperazinyl morpholinyl and mono- and di- $(C_1-C_6$ alkyl)amino, each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino,  $C_1-C_4$ alkyl,  $C_1-C_4$ haloalkyl,  $C_1-C_4$ alkoxy,  $C_1-C_4$ haloalkoxy and  $C_1-C_4$ alkylthio.

18. A compound or salt according to claim 17, wherein  $J_1$  is O.

19. A compound or salt according to claim 18, wherein:

X and Z are independently N or CH;

G is N; and

$R_2$  and  $R_3$  are independently halogen,  $C_1-C_4$ alkyl or  $C_1-C_4$ haloalkyl.

20. A compound or salt according to claim 1, wherein the compound is selected from:

N-[4-*tert*-Butyl-3-(2-hydroxy-ethoxy)-phenyl]-4-(3-trifluoromethyl-pyridin-2-yl)-benzamide;

N-[4-*tert*-Butyl-3-(2-morpholin-4-yl-ethoxy)-phenyl]-4-(3-trifluoromethyl-pyridin-2-yl)-benzamide;

N-[4-*tert*-Butyl-3-[2-(2,6-dimethyl-morpholin-4-yl)-ethoxy]-phenyl]-4-(3-trifluoromethyl-pyridin-2-yl)-benzamide (cis);

N-[4-*tert*-Butyl-3-(2-piperidin-1-yl-ethoxy)-phenyl]-4-(3-trifluoromethyl-pyridin-2-yl)-benzamide;

N-[3-{2-[Bis-(2-methoxy-ethyl)-amino]-ethoxy}-4-*tert*-butyl-phenyl]-4-(3-trifluoromethyl-pyridin-2-yl)-benzamide;

N-[4-*tert*-Butyl-3-[2-(3,3-dimethyl-piperidin-1-yl)-ethoxy]-phenyl]-4-(3-trifluoromethyl-pyridin-2-yl)-benzamide;

N-[4-*tert*-Butyl-3-(2-hydroxy-ethoxy)-phenyl]-2-hydroxy-4-(3-trifluoromethyl-pyridin-2-yl)-benzamide;

N-[4-*tert*-Butyl-3-[2-(2,6-dimethyl-morpholin-4-yl)-ethoxy]-phenyl]-2-hydroxy-4-(3-trifluoromethyl-pyridin-2-yl)-benzamide (cis); and

N-[4-*tert*-Butyl-3-(2-piperidin-1-yl-ethoxy)-phenyl]-2-hydroxy-4-(3-trifluoromethyl-pyridin-2-yl)-benzamide.

21. A compound or salt according to any one of claims 1-20, wherein the compound exhibits no detectable agonist activity an *in vitro* assay of capsaicin receptor agonism.

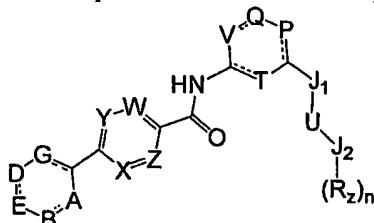
22. A compound or salt according to any one of claims 1-20, wherein the compound has an  $IC_{50}$  value of 1 micromolar or less in a capsaicin receptor calcium mobilization assay.

23. A compound or salt according to claim 22, wherein the compound has an  $IC_{50}$  value of 100 nanomolar or less in a capsaicin receptor calcium mobilization assay.

24. A pharmaceutical composition, comprising at least one compound or salt according to any one of claims 1-20, in combination with a physiologically acceptable carrier or excipient.

25. A pharmaceutical composition according to claim 24 wherein the composition is formulated as an injectible fluid, an aerosol, a cream, a gel, a pill, a capsule, a syrup or a transdermal patch.

26. A method for reducing calcium conductance of a cellular capsaicin receptor, comprising contacting a cell expressing a capsaicin receptor with at least one compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

each  $=$  independently represents a single or double bond;

either: (a) A, B and E are independently  $CR_1$ ,  $C(R_1)_2$ ,  $NR_1$  or N; or

(b) B is joined with A or E to form a fused 5- to 8-membered partially saturated ring that substituted with from 0 to 3 substituents independently selected from  $R_1$ , and the other of A or E  $CR_1$ ,  $C(R_1)_2$ ,  $NR_1$  or N;

D and G are independently  $CR_1$ ,  $C(R_1)_2$ ,  $NR_1$  or N;

W, X, Y and Z are independently  $CR_1$  or N;

P, Q, T and V are independently  $CR_1$ ,  $C(R_1)_2$ , N or NH; or Q is taken together with V or P to form a fused to 7-membered carbocycle or heterocycle that is substituted with from 0 to 4 substituents independently chosen from  $R_b$ ;

$R_1$  is independently chosen at each occurrence from hydrogen, halogen, hydroxy, amino, cyano, nitro, and groups of the formula L-M;

L is independently chosen at each occurrence from a single covalent bond, O,  $C(=O)$ ,  $OC(=O)$ ,  $C(=O)O$ ,  $OC(=O)O$ ,  $S(O)_m$ ,  $N(R_x)$ ,  $C(=O)N(R_x)$ ,  $N(R_x)C(=O)$ ,  $N(R_x)S(O)_m$ ,  $S(O)_mN(R_x)$  and  $N[S(O)_mR_x]S(O)_m$ ; wherein m is independently selected at each occurrence from 0, 1 and 2; and  $R_x$  is independently selected at each occurrence from hydrogen and  $C_1-C_8$ alkyl;

M is independently selected at each occurrence from (a) hydrogen; and (b)  $C_1-C_8$ alkyl,  $C_2-C_8$ alkenyl,  $C_2-C_8$ alkynyl, mono- and di- $(C_1-C_4$ alkyl)amino $C_0-C_4$ alkyl, phenyl $C_0-C_4$ alkyl,  $C_3-C_8$ cycloalkyl $C_0-C_4$ alkyl, (5-membered heteroaryl) $C_0-C_4$ alkyl and (5- to 7-membered heterocycloalkyl) $C_0-C_4$ alkyl, each of which is substituted with from 0 to 5 substituents independently selected from  $R_b$ ;

$J_1$  chosen from O, NH and S;

U is C<sub>1</sub>-C<sub>3</sub>alkyl, substituted with from 0 to 3 substituents independently chosen from oxo and C<sub>1</sub>-C<sub>3</sub>alkyl, or two substituents are taken together to form a 3- to 7-membered cycloalkyl or heterocycloalkyl;

Either: (a) J<sub>2</sub> is O or S,

n is 1, and

R<sub>z</sub> is hydrogen, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>haloalkyl or C<sub>2</sub>-C<sub>6</sub>alkyl ether; or

(b) J<sub>2</sub> is N,

n is 2, and

(i) R<sub>z</sub> is independently chosen at each occurrence from hydrogen and C<sub>1</sub>-C<sub>6</sub>alkyl substituted with from 0 to 3 substituents selected from R<sub>b</sub>; or

(ii) both R<sub>z</sub> moieties are joined to form, with J<sub>2</sub>, a 5- to 8-membered heterocycloalkyl that is substituted with from 0 to 3 substituents selected from R<sub>b</sub>; and

R<sub>b</sub> is independently chosen at each occurrence from halogen, hydroxy, cyano, nitro, amino, oxo, COOH, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>3</sub>-C<sub>8</sub>cycloalkylC<sub>0</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>haloalkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>1</sub>-C<sub>6</sub>haloalkoxy, C<sub>2</sub>-C<sub>6</sub>alkyl ether, aminocarbonyl, C<sub>1</sub>-C<sub>6</sub>hydroxyalkyl, C<sub>1</sub>-C<sub>6</sub>aminoalkyl and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino; and thereby reducing calcium conductance of the capsaicin receptor.

27. A method according to claim 26, wherein the compound is a compound according to claim any one of claims 1-20.

28. A method according to claim 26, wherein the cell is contacted *in vivo* in an animal.

29. A method according to claim 28, wherein the cell is a neuronal cell.

30. A method according to claim 28, wherein the cell is a urothelial cell.

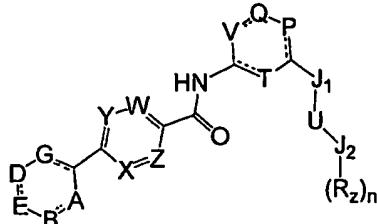
31. A method according to claim 28, wherein during contact the compound is present within a body fluid of the animal.

32. A method according to claim 31, wherein the compound is present in the blood of the animal at a concentration of 1 micromolar or less.

33. A method according to claim 28, wherein the animal is a human.

34. A method according to claim 28, wherein the compound is administered orally.

35. A method for inhibiting binding of vanilloid ligand to a capsaicin receptor *in vitro*, the method comprising contacting capsaicin receptor with at least one compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

each  $\text{---}$  independently represents a single or double bond;

either: (a) A, B and E are independently  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ ,  $\text{NR}_1$  or N; or

(b) B is joined with A or E to form a fused 5- to 8-membered partially saturated ring that is substituted with from 0 to 3 substituents independently selected from  $\text{R}_1$ , and the other of A or E is  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ ,  $\text{NR}_1$  or N;

D and G are independently  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ ,  $\text{NR}_1$  or N;

W, X, Y and Z are independently CR<sub>1</sub> or N;

P, Q, T and V are independently  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ , N or NH; or Q is taken together with V or P to form a fused to 7-membered carbocycle or heterocycle that is substituted with from 0 to 4 substituents independently chosen from  $\text{R}_b$ ;

$\text{R}_1$  is independently chosen at each occurrence from hydrogen, halogen, hydroxy, amino, cyano, nitro, and groups of the formula L-M;

L is independently chosen at each occurrence from a single covalent bond, O,  $\text{C}=\text{O}$ ,  $\text{OC}=\text{O}$ ,  $\text{C}(\text{=O})\text{O}$ ,  $\text{OC}(\text{=O})\text{O}$ ,  $\text{S}(\text{O})_m$ ,  $\text{N}(\text{R}_x)$ ,  $\text{C}(\text{=O})\text{N}(\text{R}_x)$ ,  $\text{N}(\text{R}_x)\text{C}(\text{=O})$ ,  $\text{N}(\text{R}_x)\text{S}(\text{O})_m$ ,  $\text{S}(\text{O})_m\text{N}(\text{R}_x)$  and  $\text{N}[\text{S}(\text{O})_m\text{R}_x]\text{S}(\text{O})_m$ ; wherein m is independently selected at each occurrence from 0, 1 and 2; and  $\text{R}_x$  is independently selected at each occurrence from hydrogen and  $\text{C}_1\text{-C}_8\text{alkyl}$ ;

M is independently selected at each occurrence from (a) hydrogen; and (b)  $\text{C}_1\text{-C}_8\text{alkyl}$ ,  $\text{C}_2\text{-C}_8\text{alkenyl}$ ,  $\text{C}_2\text{-C}_8\text{alkynyl}$ , mono- and di- $(\text{C}_1\text{-C}_4\text{alkyl})\text{aminoC}_0\text{-C}_4\text{alkyl}$ , phenyl $\text{C}_0\text{-C}_4\text{alkyl}$ ,  $\text{C}_3\text{-C}_8\text{cycloalkylC}_0\text{-C}_4\text{alkyl}$ ,  $(5\text{-membered heteroaryl})\text{C}_0\text{-C}_4\text{alkyl}$  and  $(5\text{- to 7-membered heterocycloalkyl})\text{C}_0\text{-C}_4\text{alkyl}$ , each of which is substituted with from 0 to 5 substituents independently selected from  $\text{R}_b$ ;

$\text{J}_1$  chosen from O, NH and S;

U is  $\text{C}_1\text{-C}_3\text{alkyl}$ , substituted with from 0 to 3 substituents independently chosen from oxo and  $\text{C}_1\text{-C}_3\text{alkyl}$ , or two substituents are taken together to form a 3- to 7-membered cycloalkyl or heterocycloalkyl;

Either: (a)  $\text{J}_2$  is O or S,

n is 1, and

$\text{R}_2$  is hydrogen,  $\text{C}_1\text{-C}_6\text{alkyl}$ ,  $\text{C}_1\text{-C}_6\text{haloalkyl}$  or  $\text{C}_2\text{-C}_6\text{alkyl}$  ether; or

(b)  $\text{J}_2$  is N,

n is 2, and

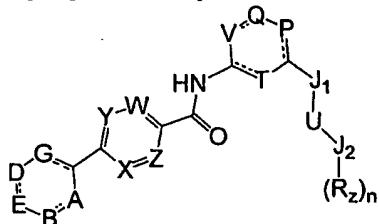
(i) R<sub>z</sub> is independently chosen at each occurrence from hydrogen and C<sub>1</sub>-C<sub>6</sub>alkyl substituted with from 0 to 3 substituents selected from R<sub>b</sub>; or

(ii) both R<sub>z</sub> moieties are joined to form, with J<sub>2</sub>, a 5- to 8-membered heterocycloalkyl that is substituted with from 0 to 3 substituents selected from R<sub>b</sub>; and

R<sub>b</sub> is independently chosen at each occurrence from halogen, hydroxy, cyano, nitro, amino, oxo, COOH, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>3</sub>-C<sub>8</sub>cycloalkylC<sub>0</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>haloalkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>1</sub>-C<sub>6</sub>haloalkoxy, C<sub>2</sub>-C<sub>6</sub>alkyl ether, aminocarbonyl, C<sub>1</sub>-C<sub>6</sub>hydroxyalkyl, C<sub>1</sub>-C<sub>6</sub>aminoalkyl and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino; under conditions and in an amount sufficient to detectably inhibit vanilloid ligand binding to capsaicin receptor.

36. A method according to claim 35, wherein the compound is a compound according to claim any one of claims 1-20.

37. A method for inhibiting binding of vanilloid ligand to capsaicin receptor in a patient, comprising contacting cells expressing capsaicin receptor with at least one compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

each --- independently represents a single or double bond;

either: (a) A, B and E are independently CR<sub>1</sub>, C(R<sub>1</sub>)<sub>2</sub>, NR<sub>1</sub> or N; or

(b) B is joined with A or E to form a fused 5- to 8-membered partially saturated ring that is substituted with from 0 to 3 substituents independently selected from R<sub>1</sub>, and the other of A or E CR<sub>1</sub>, C(R<sub>1</sub>)<sub>2</sub>, NR<sub>1</sub> or N;

D and G are independently CR<sub>1</sub>, C(R<sub>1</sub>)<sub>2</sub>, NR<sub>1</sub> or N;

W, X, Y and Z are independently CR<sub>1</sub> or N;

P, Q, T and V are independently CR<sub>1</sub>, C(R<sub>1</sub>)<sub>2</sub>, N or NH; or Q is taken together with V or P to form a fused to 7-membered carbocycle or heterocycle that is substituted with from 0 to 4 substituents independently chosen from R<sub>b</sub>;

R<sub>1</sub> is independently chosen at each occurrence from hydrogen, halogen, hydroxy, amino, cyano, nitro, and groups of the formula L-M;

L is independently chosen at each occurrence from a single covalent bond, O, C(=O), OC(=O), C(=O)O, OC(=O)O, S(O)<sub>m</sub>, N(R<sub>x</sub>), C(=O)N(R<sub>x</sub>), N(R<sub>x</sub>)C(=O), N(R<sub>x</sub>)S(O)<sub>m</sub>, S(O)<sub>m</sub>N(R<sub>x</sub>) and

$N[S(O)_mR_x]S(O)_m$ ; wherein  $m$  is independently selected at each occurrence from 0, 1 and 2; and  $R_x$  is independently selected at each occurrence from hydrogen and  $C_1$ - $C_8$ alkyl;

$M$  is independently selected at each occurrence from (a) hydrogen; and (b)  $C_1$ - $C_8$ alkyl,  $C_2$ - $C_8$ alkenyl,  $C_2$ - $C_8$ alkynyl, mono- and di- $(C_1$ - $C_4$ alkyl)amino $C_0$ - $C_4$ alkyl, phenyl $C_0$ - $C_4$ alkyl,  $C_3$ - $C_8$ cycloalkyl $C_0$ - $C_4$ alkyl, (5-membered heteroaryl) $C_0$ - $C_4$ alkyl and (5- to 7-membered heterocycloalkyl) $C_0$ - $C_4$ alkyl, each of which is substituted with from 0 to 5 substituents independently selected from  $R_b$ ;

$J_1$  chosen from O, NH and S;

$U$  is  $C_1$ - $C_3$ alkyl, substituted with from 0 to 3 substituents independently chosen from oxo and  $C_1$ - $C_3$ alkyl, or two substituents are taken together to form a 3- to 7-membered cycloalkyl or heterocycloalkyl;

Either: (a)  $J_2$  is O or S,

$n$  is 1, and

$R_z$  is hydrogen,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ haloalkyl or  $C_2$ - $C_6$ alkyl ether; or

(b)  $J_2$  is N,

$n$  is 2, and

(i)  $R_z$  is independently chosen at each occurrence from hydrogen and  $C_1$ - $C_6$ alkyl substituted with from 0 to 3 substituents selected from  $R_b$ ; or

(ii) both  $R_z$  moieties are joined to form, with  $J_2$ , a 5- to 8-membered heterocycloalkyl that is substituted with from 0 to 3 substituents selected from  $R_b$ ; and

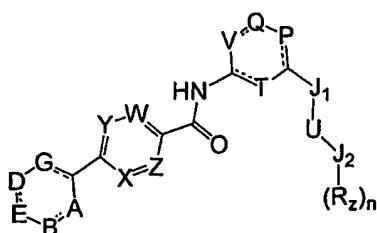
$R_b$  is independently chosen at each occurrence from halogen, hydroxy, cyano, nitro, amino, oxo, COOH,  $C_1$ - $C_6$ alkyl,  $C_3$ - $C_8$ cycloalkyl $C_0$ - $C_4$ alkyl,  $C_1$ - $C_6$ haloalkyl,  $C_1$ - $C_6$ alkoxy,  $C_1$ - $C_6$ haloalkoxy,  $C_2$ - $C_6$ alkyl ether, aminocarbonyl,  $C_1$ - $C_6$ hydroxyalkyl,  $C_1$ - $C_6$ aminoalkyl and mono- and di- $(C_1$ - $C_6$ alkyl)amino;

and thereby inhibiting binding of vanilloid ligand to the capsaicin receptor in the patient.

38. A method according to claim 37, wherein the compound is a compound according to claim any one of claims 1-20.

39. A method according to claim 37, wherein the patient is a human.

40. A method for treating a condition responsive to capsaicin receptor modulation in a patient, comprising administering to the patient a therapeutically effective amount of at least one compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

each  $\text{---}$  independently represents a single or double bond;

either: (a) A, B and E are independently  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ ,  $\text{NR}_1$  or N; or

(b) B is joined with A or E to form a fused 5- to 8-membered partially saturated ring that substituted with from 0 to 3 substituents independently selected from  $\text{R}_1$ , and the other of A or E  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ ,  $\text{NR}_1$  or N;

D and G are independently  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ ,  $\text{NR}_1$  or N;

W, X, Y and Z are independently  $\text{CR}_1$  or N;

P, Q, T and V are independently  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ , N or NH; or Q is taken together with V or P to form a fused to 7-membered carbocycle or heterocycle that is substituted with from 0 to 4 substituents independent chosen from  $\text{R}_b$ ;

$\text{R}_1$  is independently chosen at each occurrence from hydrogen, halogen, hydroxy, amino, cyano, nitro, and groups of the formula L-M;

L is independently chosen at each occurrence from a single covalent bond, O,  $\text{C}(=\text{O})$ ,  $\text{OC}(=\text{O})$ ,  $\text{C}(=\text{O})\text{O}$ ,  $\text{OC}(=\text{O})\text{O}$ ,  $\text{S}(\text{O})_m$ ,  $\text{N}(\text{R}_x)$ ,  $\text{C}(=\text{O})\text{N}(\text{R}_x)$ ,  $\text{N}(\text{R}_x)\text{C}(=\text{O})$ ,  $\text{N}(\text{R}_x)\text{S}(\text{O})_m$ ,  $\text{S}(\text{O})_m\text{N}(\text{R}_x)$  and  $\text{N}[\text{S}(\text{O})_m\text{R}_x]\text{S}(\text{O})_m$ ; wherein m is independently selected at each occurrence from 0, 1 and 2; and  $\text{R}_x$  is independently selected at each occurrence from hydrogen and  $\text{C}_1\text{-C}_8\text{alkyl}$ ;

M is independently selected at each occurrence from (a) hydrogen; and (b)  $\text{C}_1\text{-C}_8\text{alkyl}$ ,  $\text{C}_2\text{-C}_8\text{alkenyl}$ ,  $\text{C}_2\text{-C}_8\text{alkynyl}$ , mono- and di- $(\text{C}_1\text{-C}_4\text{alkyl})\text{aminoC}_0\text{-C}_4\text{alkyl}$ ,  $\text{phenylC}_0\text{-C}_4\text{alkyl}$ ,  $\text{C}_3\text{-C}_8\text{cycloalkylC}_0\text{-C}_4\text{alkyl}$ ,  $(5\text{-membered heteroaryl})\text{C}_0\text{-C}_4\text{alkyl}$  and  $(5\text{- to 7-membered heterocycloalkyl})\text{C}_0\text{-C}_4\text{alkyl}$ , each of which is substituted with from 0 to 5 substituents independently selected from  $\text{R}_b$ ;

$\text{J}_1$  chosen from O, NH and S;

U is  $\text{C}_1\text{-C}_3\text{alkyl}$ , substituted with from 0 to 3 substituents independently chosen from oxo and  $\text{C}_1\text{-C}_3\text{alkyl}$ , or two substituents are taken together to form a 3- to 7-membered cycloalkyl or heterocycloalkyl;

Either: (a)  $\text{J}_2$  is O or S,

n is 1, and

$\text{R}_z$  is hydrogen,  $\text{C}_1\text{-C}_6\text{alkyl}$ ,  $\text{C}_1\text{-C}_6\text{haloalkyl}$  or  $\text{C}_2\text{-C}_6\text{alkyl}$  ether; or

(b)  $\text{J}_2$  is N,

n is 2, and

(i)  $\text{R}_z$  is independently chosen at each occurrence from hydrogen and  $\text{C}_1\text{-C}_6\text{alkyl}$  substituted with from 0 to 3 substituents selected from  $\text{R}_b$ ; or

(ii) both  $\text{R}_z$  moieties are joined to form, with  $\text{J}_2$ , a 5- to 8-membered heterocycloalkyl that is substituted with from 0 to 3 substituents selected from  $\text{R}_b$ ; and

$\text{R}_b$  is independently chosen at each occurrence from halogen, hydroxy, cyano, nitro, amino, oxo, COOH,  $\text{C}_1\text{-C}_6\text{alkyl}$ ,  $\text{C}_3\text{-C}_8\text{cycloalkylC}_0\text{-C}_4\text{alkyl}$ ,  $\text{C}_1\text{-C}_6\text{haloalkyl}$ ,  $\text{C}_1\text{-C}_6\text{alkoxy}$ ,  $\text{C}_1\text{-C}_6\text{haloalkoxy}$ ,  $\text{C}_2\text{-C}_6\text{alkyl}$  ether, aminocarbonyl,  $\text{C}_1\text{-C}_6\text{hydroxyalkyl}$ ,  $\text{C}_1\text{-C}_6\text{aminoalkyl}$  and mono- and di- $(\text{C}_1\text{-C}_6\text{alkyl})\text{amino}$ ;

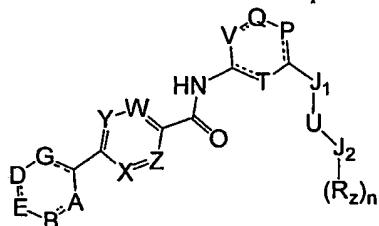
and thereby alleviating the condition in the patient.

41. A method according to claim 40, wherein the compound is a compound according to claim any one of claims 1-20.

42. A method according to claim 40, wherein the patient is suffering from (i) exposure to capsaicin, (ii) burn or irritation due to exposure to heat, (iii) burns or irritation due to exposure to light, (iv) burn, bronchoconstriction or irritation due to exposure to tear gas, air pollutants, infectious agents or pepper spray, or (v) burn or irritation due to exposure to acid

43. A method according to claim 40, wherein the condition is asthma or chronic obstructive pulmonary disease.

44. A method for treating pain in a patient, comprising administering to a patient suffering from pain a therapeutically effective amount of at least one compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

each  $\text{---}$  independently represents a single or double bond;

either: (a) A, B and E are independently  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ ,  $\text{NR}_1$  or N; or

(b) B is joined with A or E to form a fused 5- to 8-membered partially saturated ring that is substituted with from 0 to 3 substituents independently selected from  $\text{R}_1$ , and the other of A or E is  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ ,  $\text{NR}_1$  or N;

D and G are independently  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ ,  $\text{NR}_1$  or N;

W, X, Y and Z are independently  $\text{CR}_1$  or N;

P, Q, T and V are independently  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ , N or NH; or Q is taken together with V or P to form a fused to 7-membered carbocycle or heterocycle that is substituted with from 0 to 4 substituents independently chosen from  $\text{R}_b$ ;

$\text{R}_1$  is independently chosen at each occurrence from hydrogen, halogen, hydroxy, amino, cyano, nitro, and groups of the formula L-M;

L is independently chosen at each occurrence from a single covalent bond, O,  $\text{C}=\text{O}$ ,  $\text{OC}=\text{O}$ ,  $\text{C}(\text{=O})\text{O}$ ,  $\text{OC}(\text{=O})\text{O}$ ,  $\text{S}(\text{O})_m$ ,  $\text{N}(\text{R}_x)$ ,  $\text{C}(\text{=O})\text{N}(\text{R}_x)$ ,  $\text{N}(\text{R}_x)\text{C}(\text{=O})$ ,  $\text{N}(\text{R}_x)\text{S}(\text{O})_m$ ,  $\text{S}(\text{O})_m\text{N}(\text{R}_x)$  and  $\text{N}[\text{S}(\text{O})_m\text{R}_x]\text{S}(\text{O})_m$ ; wherein m is independently selected at each occurrence from 0, 1 and 2; and  $\text{R}_x$  is independently selected at each occurrence from hydrogen and  $\text{C}_1\text{-C}_8$ alkyl;

M is independently selected at each occurrence from (a) hydrogen; and (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl, phenylC<sub>0</sub>-C<sub>4</sub>alkyl, C<sub>3</sub>-C<sub>8</sub>cycloalkylC<sub>0</sub>-C<sub>4</sub>alkyl, (5-membered heteroaryl)C<sub>0</sub>-C<sub>4</sub>alkyl and (5- to 7-membered heterocycloalkyl)C<sub>0</sub>-C<sub>4</sub>alkyl, each of which is substituted with from 0 to 5 substituents independently selected from R<sub>b</sub>;

J<sub>1</sub> chosen from O, NH and S;

U is C<sub>1</sub>-C<sub>3</sub>alkyl, substituted with from 0 to 3 substituents independently chosen from oxo and C<sub>1</sub>-C<sub>3</sub>alkyl, or two substituents are taken together to form a 3- to 7-membered cycloalkyl or heterocycloalkyl;

Either: (a) J<sub>2</sub> is O or S,

n is 1, and

R<sub>z</sub> is hydrogen, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>haloalkyl or C<sub>2</sub>-C<sub>6</sub>alkyl ether; or

(b) J<sub>2</sub> is N,

n is 2, and

(i) R<sub>z</sub> is independently chosen at each occurrence from hydrogen and C<sub>1</sub>-C<sub>6</sub>alkyl substituted with from 0 to 3 substituents selected from R<sub>b</sub>; or

(ii) both R<sub>z</sub> moieties are joined to form, with J<sub>2</sub>, a 5- to 8-membered heterocycloalkyl that is substituted with from 0 to 3 substituents selected from R<sub>b</sub>; and

R<sub>b</sub> is independently chosen at each occurrence from halogen, hydroxy, cyano, nitro, amino, oxo, COOH, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>3</sub>-C<sub>8</sub>cycloalkylC<sub>0</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>haloalkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>1</sub>-C<sub>6</sub>haloalkoxy, C<sub>2</sub>-C<sub>6</sub>alkyl ether, aminocarbonyl, C<sub>1</sub>-C<sub>6</sub>hydroxyalkyl, C<sub>1</sub>-C<sub>6</sub>aminoalkyl and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino; and thereby alleviating pain in the patient.

45. A method according to claim 44, wherein the compound is a compound according to claim any one of claims 1-20.

46. A method according to claim 44, wherein the compound is present in the blood of the patient at a concentration of 1 micromolar or less.

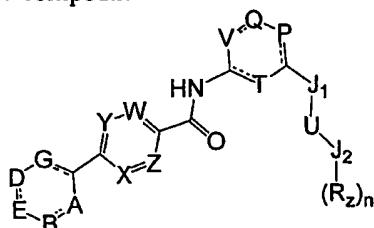
47. A method according to claim 44, wherein the patient is suffering from neuropathic pain.

48. A method according to claim 44, wherein the pain is associated with a condition selected from: postmastectomy pain syndrome, stump pain, phantom limb pain, oral neuropathic pain, toothache, postherpetic neuralgia, diabetic neuropathy, reflex sympathetic dystrophy, trigeminal neuralgia, osteoarthritis, rheumatoid arthritis, fibromyalgia, Guillain-Barre syndrome, meralgia paresthetica, burning-mouth syndrome, bilateral peripheral neuropathy, causalgia, neuritis, neuronitis, neuralgia, AIDS-related neuropathy, MS-related neuropathy, spinal cord injury-related pain, surgery-related pain, musculoskeletal pain, back pain, headache, migraine, angina, labor, hemorrhoids, dyspepsia, Charcot's

pains, intestinal gas, menstruation, cancer, venom exposure, irritable bowel syndrome, inflammatory bowel disease and trauma.

49. A method according to claim 44, wherein the patient is a human.

50. A method for treating itch in a patient, comprising administering to a patient a therapeutically effective amount of a compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

each  $\text{---}$  independently represents a single or double bond;

either: (a) A, B and E are independently  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ ,  $\text{NR}_1$  or N; or

(b) B is joined with A or E to form a fused 5- to 8-membered partially saturated ring that substituted with from 0 to 3 substituents independently selected from  $\text{R}_1$ , and the other of A or E  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ ,  $\text{NR}_1$  or N;

D and G are independently  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ ,  $\text{NR}_1$  or N;

W, X, Y and Z are independently  $\text{CR}_1$  or N;

P, Q, T and V are independently  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ , N or NH; or Q is taken together with V or P to form a fused to 7-membered carbocycle or heterocycle that is substituted with from 0 to 4 substituents independent chosen from  $\text{R}_8$ ;

$\text{R}_1$  is independently chosen at each occurrence from hydrogen, halogen, hydroxy, amino, cyano, nitro, and groups of the formula L-M;

L is independently chosen at each occurrence from a single covalent bond, O,  $\text{C}(=\text{O})$ ,  $\text{OC}(=\text{O})$ ,  $\text{C}(=\text{O})\text{O}$ ,  $\text{OC}(=\text{O})\text{O}$ ,  $\text{S}(\text{O})_m$ ,  $\text{N}(\text{R}_x)$ ,  $\text{C}(=\text{O})\text{N}(\text{R}_x)$ ,  $\text{N}(\text{R}_x)\text{C}(=\text{O})$ ,  $\text{N}(\text{R}_x)\text{S}(\text{O})_m$ ,  $\text{S}(\text{O})_m\text{N}(\text{R}_x)$  and  $\text{N}[\text{S}(\text{O})_m\text{R}_x]\text{S}(\text{O})_m$ ; wherein m is independently selected at each occurrence from 0, 1 and 2; and  $\text{R}_x$  is independently selected at each occurrence from hydrogen and  $\text{C}_1\text{-C}_8$ alkyl;

M is independently selected at each occurrence from (a) hydrogen; and (b)  $\text{C}_1\text{-C}_8$ alkyl,  $\text{C}_2\text{-C}_8$ alkenyl,  $\text{C}_2\text{-C}_8$ alkynyl, mono- and di- $(\text{C}_1\text{-C}_4$ alkyl)amino $\text{C}_0\text{-C}_4$ alkyl, phenyl $\text{C}_0\text{-C}_4$ alkyl,  $\text{C}_3\text{-C}_8$ cycloalkyl $\text{C}_0\text{-C}_4$ alkyl, (5-membered heteroaryl) $\text{C}_0\text{-C}_4$ alkyl and (5- to 7-membered heterocycloalkyl) $\text{C}_0\text{-C}_4$ alkyl, each of which is substituted with from 0 to 5 substituents independently selected from  $\text{R}_b$ ;

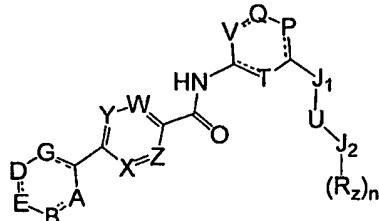
$\text{J}_1$  chosen from O, NH and S;

$\text{U}$  is  $\text{C}_1\text{-C}_3$ alkyl, substituted with from 0 to 3 substituents independently chosen from oxo and  $\text{C}_1\text{-C}_3$ alkyl, or two substituents are taken together to form a 3- to 7-membered cycloalkyl or heterocycloalkyl;

Either: (a)  $J_2$  is O or S,  
 $n$  is 1, and  
 $R_2$  is hydrogen,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ haloalkyl or  $C_2$ - $C_6$ alkyl ether; or  
(b)  $J_2$  is N,  
 $n$  is 2, and  
(i)  $R_2$  is independently chosen at each occurrence from hydrogen and  $C_1$ - $C_6$ alkyl substituted with from 0 to 3 substituents selected from  $R_b$ ; or  
(ii) both  $R_2$  moieties are joined to form, with  $J_2$ , a 5- to 8-membered heterocycloalkyl that is substituted with from 0 to 3 substituents selected from  $R_b$ ; and  
 $R_b$  is independently chosen at each occurrence from halogen, hydroxy, cyano, nitro, amino, oxo, COOH,  $C_1$ - $C_6$ alkyl,  $C_3$ - $C_8$ cycloalkyl $C_0$ - $C_4$ alkyl,  $C_1$ - $C_6$ haloalkyl,  $C_1$ - $C_6$ alkoxy,  $C_1$ - $C_6$ haloalkoxy,  $C_2$ - $C_6$ alkyl ether, aminocarbonyl,  $C_1$ - $C_6$ hydroxyalkyl,  $C_1$ - $C_6$ aminoalkyl and mono- and di- $(C_1$ - $C_6$ alkyl)amino; and thereby alleviating itch in the patient.

51. A method according to claim 50, wherein the compound is a compound according to claim any one of claims 1-20.

52. A method for treating cough or hiccup in a patient, comprising administering to a patient a therapeutically effective amount of a compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

each  $---$  independently represents a single or double bond;

either: (a) A, B and E are independently  $CR_1$ ,  $C(R_1)_2$ ,  $NR_1$  or N; or

(b) B is joined with A or E to form a fused 5- to 8-membered partially saturated ring that is substituted with from 0 to 3 substituents independently selected from  $R_1$ , and the other of A or E is  $CR_1$ ,  $C(R_1)_2$ ,  $NR_1$  or N;

D and G are independently  $CR_1$ ,  $C(R_1)_2$ ,  $NR_1$  or N;

W, X, Y and Z are independently CR<sub>1</sub> or N;

P, Q, T and V are independently CR<sub>1</sub>, C(R<sub>1</sub>)<sub>2</sub>, N or NH; or Q is taken together with V or P to form a fused to 7-membered carbocycle or heterocycle that is substituted with from 0 to 4 substituents independently chosen from R<sub>b</sub>;

R<sub>1</sub> is independently chosen at each occurrence from hydrogen, halogen, hydroxy, amino, cyano, nitro, and groups of the formula L-M;

L is independently chosen at each occurrence from a single covalent bond, O, C(=O), OC(=O), C(=O)O, OC(=O)O, S(O)<sub>m</sub>, N(R<sub>x</sub>), C(=O)N(R<sub>x</sub>), N(R<sub>x</sub>)C(=O), N(R<sub>x</sub>)S(O)<sub>m</sub>, S(O)<sub>m</sub>N(R<sub>x</sub>) and N[S(O)<sub>m</sub>R<sub>x</sub>]S(O)<sub>m</sub>; wherein m is independently selected at each occurrence from 0, 1 and 2; and R<sub>x</sub> is independently selected at each occurrence from hydrogen and C<sub>1</sub>-C<sub>8</sub>alkyl;

M is independently selected at each occurrence from (a) hydrogen; and (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl, phenylC<sub>0</sub>-C<sub>4</sub>alkyl, C<sub>3</sub>-C<sub>8</sub>cycloalkylC<sub>0</sub>-C<sub>4</sub>alkyl, (5-membered heteroaryl)C<sub>0</sub>-C<sub>4</sub>alkyl and (5- to 7-membered heterocycloalkyl)C<sub>0</sub>-C<sub>4</sub>alkyl, each of which is substituted with from 0 to 5 substituents independently selected from R<sub>b</sub>;

J<sub>1</sub> chosen from O, NH and S;

U is C<sub>1</sub>-C<sub>3</sub>alkyl, substituted with from 0 to 3 substituents independently chosen from oxo and C<sub>1</sub>-C<sub>3</sub>alkyl, or two substituents are taken together to form a 3- to 7-membered cycloalkyl or heterocycloalkyl;

Either: (a) J<sub>2</sub> is O or S,

n is 1, and

R<sub>z</sub> is hydrogen, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>haloalkyl or C<sub>2</sub>-C<sub>6</sub>alkyl ether; or

(b) J<sub>2</sub> is N,

n is 2, and

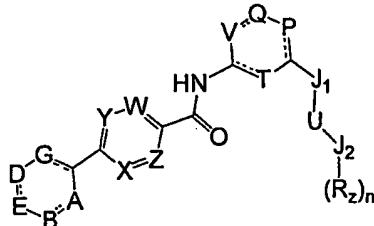
(i) R<sub>z</sub> is independently chosen at each occurrence from hydrogen and C<sub>1</sub>-C<sub>6</sub>alkyl substituted with from 0 to 3 substituents selected from R<sub>b</sub>; or

(ii) both R<sub>z</sub> moieties are joined to form, with J<sub>2</sub>, a 5- to 8-membered heterocycloalkyl that is substituted with from 0 to 3 substituents selected from R<sub>b</sub>; and

R<sub>b</sub> is independently chosen at each occurrence from halogen, hydroxy, cyano, nitro, amino, oxo, COOH, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>3</sub>-C<sub>8</sub>cycloalkylC<sub>0</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>haloalkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>1</sub>-C<sub>6</sub>haloalkoxy, C<sub>2</sub>-C<sub>6</sub>alkyl ether, aminocarbonyl, C<sub>1</sub>-C<sub>6</sub>hydroxyalkyl, C<sub>1</sub>-C<sub>6</sub>aminoalkyl and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino; and thereby alleviating cough or hiccup in the patient.

53. A method according to claim 52, wherein the compound is a compound according to claim any one of claims 1-20.

54. A method for treating urinary incontinence or overactive bladder in a patient, comprising administering to a patient a therapeutically effective amount of a compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

each  $\text{---}$  independently represents a single or double bond;

either: (a) A, B and E are independently  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ ,  $\text{NR}_1$  or N; or

(b) B is joined with A or E to form a fused 5- to 8-membered partially saturated ring that is substituted with from 0 to 3 substituents independently selected from  $\text{R}_1$ , and the other of A or E is  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ ,  $\text{NR}_1$  or N;

D and G are independently  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ ,  $\text{NR}_1$  or N;

W, X, Y and Z are independently  $\text{CR}_1$  or N;

P, Q, T and V are independently  $\text{CR}_1$ ,  $\text{C}(\text{R}_1)_2$ , N or NH; or Q is taken together with V or P to form a fused 5- to 7-membered carbocycle or heterocycle that is substituted with from 0 to 4 substituents independently selected from  $\text{R}_b$ ;

$\text{R}_1$  is independently chosen at each occurrence from hydrogen, halogen, hydroxy, amino, cyano, nitro, and groups of the formula L-M;

L is independently chosen at each occurrence from a single covalent bond, O,  $\text{C}=\text{O}$ ,  $\text{OC}(\text{=O})$ ,  $\text{C}(\text{=O})\text{O}$ ,  $\text{OC}(\text{=O})\text{O}$ ,  $\text{S}(\text{O})_m$ ,  $\text{N}(\text{R}_x)$ ,  $\text{C}(\text{=O})\text{N}(\text{R}_x)$ ,  $\text{N}(\text{R}_x)\text{C}(\text{=O})$ ,  $\text{N}(\text{R}_x)\text{S}(\text{O})_m$ ,  $\text{S}(\text{O})_m\text{N}(\text{R}_x)$  and  $\text{N}[\text{S}(\text{O})_m\text{R}_x]\text{S}(\text{O})_m$ ; wherein m is independently selected at each occurrence from 0, 1 and 2; and  $\text{R}_x$  is independently selected at each occurrence from hydrogen and  $\text{C}_1\text{-C}_8$ alkyl;

M is independently selected at each occurrence from (a) hydrogen; and (b)  $\text{C}_1\text{-C}_8$ alkyl,  $\text{C}_2\text{-C}_8$ alkenyl,  $\text{C}_2\text{-C}_8$ alkynyl, mono- and di- $(\text{C}_1\text{-C}_4$ alkyl)amino $\text{C}_0\text{-C}_4$ alkyl, phenyl $\text{C}_0\text{-C}_4$ alkyl,  $\text{C}_3\text{-C}_8$ cycloalkyl $\text{C}_0\text{-C}_4$ alkyl, (5-membered heteroaryl) $\text{C}_0\text{-C}_4$ alkyl and (5- to 7-membered heterocycloalkyl) $\text{C}_0\text{-C}_4$ alkyl, each of which is substituted with from 0 to 5 substituents independently selected from  $\text{R}_b$ ;

$\text{J}_1$  chosen from O, NH and S;

U is  $\text{C}_1\text{-C}_3$ alkyl, substituted with from 0 to 3 substituents independently chosen from oxo and  $\text{C}_1\text{-C}_3$ alkyl, or two substituents are taken together to form a 3- to 7-membered cycloalkyl or heterocycloalkyl;

Either: (a)  $\text{J}_2$  is O or S,

n is 1, and

$\text{R}_z$  is hydrogen,  $\text{C}_1\text{-C}_6$ alkyl,  $\text{C}_1\text{-C}_6$ haloalkyl or  $\text{C}_2\text{-C}_6$ alkyl ether; or

(b)  $\text{J}_2$  is N,

n is 2, and

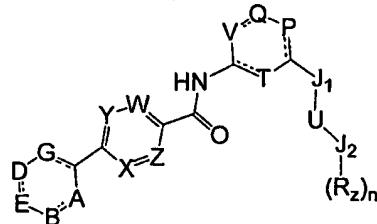
(i) R<sub>2</sub> is independently chosen at each occurrence from hydrogen and C<sub>1</sub>-C<sub>6</sub>alkyl substituted with from 0 to 3 substituents selected from R<sub>b</sub>; or

(ii) both R<sub>2</sub> moieties are joined to form, with J<sub>2</sub>, a 5- to 8-membered heterocycloalkyl that is substituted with from 0 to 3 substituents selected from R<sub>b</sub>; and

R<sub>b</sub> is independently chosen at each occurrence from halogen, hydroxy, cyano, nitro, amino, oxo, COOH C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>3</sub>-C<sub>8</sub>cycloalkylC<sub>0</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>haloalkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>1</sub>-C<sub>6</sub>haloalkoxy, C<sub>2</sub>-C<sub>6</sub>alky ether, aminocarbonyl, C<sub>1</sub>-C<sub>6</sub>hydroxyalkyl, C<sub>1</sub>-C<sub>6</sub>aminoalkyl and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino; and thereby alleviating urinary incontinence or overactive bladder in the patient.

55. A method according to claim 54, wherein the compound is a compound according to claim any one of claims 1-20.

56. A method promoting weight loss in an obese patient, comprising administering to a patient a therapeutically effective amount of a compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

each --- independently represents a single or double bond;

either: (a) A, B and E are independently CR<sub>1</sub>, C(R<sub>1</sub>)<sub>2</sub>, NR<sub>1</sub> or N; or

(b) B is joined with A or E to form a fused 5- to 8-membered partially saturated ring that is substituted with from 0 to 3 substituents independently selected from R<sub>1</sub>, and the other of A or E is CR<sub>1</sub>, C(R<sub>1</sub>)<sub>2</sub>, NR<sub>1</sub> or N;

D and G are independently CR<sub>1</sub>, C(R<sub>1</sub>)<sub>2</sub>, NR<sub>1</sub> or N;

W, X, Y and Z are independently CR<sub>1</sub> or N;

P, Q, T and V are independently CR<sub>1</sub>, C(R<sub>1</sub>)<sub>2</sub>, N or NH; or Q is taken together with V or P to form a fused to 7-membered carbocycle or heterocycle that is substituted with from 0 to 4 substituents independently chosen from R<sub>b</sub>;

R<sub>1</sub> is independently chosen at each occurrence from hydrogen, halogen, hydroxy, amino, cyano, nitro, and groups of the formula L-M;

L is independently chosen at each occurrence from a single covalent bond, O, C(=O), OC(=O), C(=O)O, OC(=O)O, S(O)<sub>m</sub>, N(R<sub>x</sub>), C(=O)N(R<sub>x</sub>), N(R<sub>x</sub>)C(=O), N(R<sub>x</sub>)S(O)<sub>m</sub>, S(O)<sub>m</sub>N(R<sub>x</sub>) and

$N[S(O)_mR_x]S(O)_m$ ; wherein  $m$  is independently selected at each occurrence from 0, 1 and 2; and  $R_x$  is independently selected at each occurrence from hydrogen and  $C_1$ - $C_8$ alkyl;

$M$  is independently selected at each occurrence from (a) hydrogen; and (b)  $C_1$ - $C_8$ alkyl,  $C_2$ - $C_8$ alkenyl,  $C_2$ - $C_8$ alkynyl, mono- and di- $(C_1$ - $C_4$ alkyl)amino $C_0$ - $C_4$ alkyl, phenyl $C_0$ - $C_4$ alkyl,  $C_3$ - $C_8$ cycloalkyl $C_0$ - $C_4$ alkyl, (5-membered heteroaryl) $C_0$ - $C_4$ alkyl and (5- to 7-membered heterocycloalkyl) $C_0$ - $C_4$ alkyl each of which is substituted with from 0 to 5 substituents independently selected from  $R_b$ ;

$J_1$  chosen from O, NH and S;

$U$  is  $C_1$ - $C_3$ alkyl, substituted with from 0 to 3 substituents independently chosen from oxo and  $C_1$ - $C_3$ alkyl or two substituents are taken together to form a 3- to 7-membered cycloalkyl or heterocycloalkyl;

Either: (a)  $J_2$  is O or S,

$n$  is 1, and

$R_z$  is hydrogen,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ haloalkyl or  $C_2$ - $C_6$ alkyl ether; or

(b)  $J_2$  is N,

$n$  is 2, and

(i)  $R_z$  is independently chosen at each occurrence from hydrogen and  $C_1$ - $C_6$ alkyl substituents with from 0 to 3 substituents selected from  $R_b$ ; or

(ii) both  $R_z$  moieties are joined to form, with  $J_2$ , a 5- to 8-membered heterocycloalkyl that is substituted with from 0 to 3 substituents selected from  $R_b$ ; and

$R_b$  is independently chosen at each occurrence from halogen, hydroxy, cyano, nitro, amino, oxo, COOH,  $C_1$ - $C_6$ alkyl,  $C_3$ - $C_8$ cycloalkyl $C_0$ - $C_4$ alkyl,  $C_1$ - $C_6$ haloalkyl,  $C_1$ - $C_6$ alkoxy,  $C_1$ - $C_6$ haloalkoxy,  $C_2$ - $C_6$ alkyl ether, aminocarbonyl,  $C_1$ - $C_6$ hydroxyalkyl,  $C_1$ - $C_6$ aminoalkyl and mono- and di- $(C_1$ - $C_6$ alkyl)amino; and thereby promoting weight loss in the patient.

57. A method according to claim 56, wherein the compound is a compound according to claim any one of claims 1-20.

58. A compound or salt according to any one of claims 1-20, wherein the compound or salt is radiolabeled.

59. A method for determining the presence or absence of capsaicin receptor in a sample comprising the steps of:

- (a) contacting a sample with a compound or salt according to any one of claims 1-20, under conditions that permit binding of the compound to capsaicin receptor; and
- (b) detecting a level of the compound bound to capsaicin receptor, and therefrom determining the presence or absence of capsaicin receptor in the sample.

60. A method according to claim 60, wherein the compound is a radiolabeled compound according to claim 58, and wherein the step of detection comprises the steps of:

- (i) separating unbound compound from bound compound; and
- (ii) detecting the presence or absence of bound compound in the sample.

61. A packaged pharmaceutical preparation, comprising:

- (a) a pharmaceutical composition according to claim 24 in a container; and
- (b) instructions for using the composition to treat pain.

62. A packaged pharmaceutical preparation, comprising:

- (a) a pharmaceutical composition according to claim 24 in a container; and
- (b) instructions for using the composition to treat cough or hiccup.

63. A packaged pharmaceutical preparation, comprising:

- (a) a pharmaceutical composition according to claim 24 in a container; and
- (b) instructions for using the composition to treat obesity.

64. A packaged pharmaceutical preparation, comprising:

- (a) a pharmaceutical composition according to claim 24 in a container; and
- (b) instructions for using the composition to treat urinary incontinence or overactive bladder.

65. The use of a compound or salt according to any one of claims 1-20 for the manufacture of a medicament for the treatment of a condition responsive to capsaicin receptor modulation.

66. A use according to claim 65, wherein the condition is pain, asthma, chronic obstructive pulmonary disease, cough, hiccup, obesity, urinary incontinence or overactive bladder, exposure to capsaicin, burn or irritation due to exposure to heat, burn or irritation due to exposure to light, burn, bronchoconstriction or irritation due to exposure to tear gas, air pollutants, infectious agents or pepper spray, or burn or irritation due to exposure to acid.